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Extremely Elevated Erythrocyte Sedimentation Rates: Associations With Patients' Diagnoses, Demographic Characteristics, and Comorbidities

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Abstract

Objective: To study associations between extreme erythrocyte sedimentation rate (ESR) elevations (≥100 mm/h) and diseases, age, sex, race, Charlson Comorbidity Index (CCI), and C-reactive protein (CRP) level.

Patients and Methods: This was a retrospective cohort study of 4807 patients with extreme ESR values examined at Mayo Clinic, Rochester, Minnesota, from January 1, 2002, through December 31, 2011. Independent variables included diseases (infection, autoimmune, malignancy, renal disease, or miscellaneous), subcategories of diseases, patient demographic characteristics (age, sex, and race), CRP level, and CCI. The Wilcoxon rank sum test was used to assess comparisons of ESR between patients with and without disease as well as relationships between extreme ESR values and demographic characteristics of patients within disease categories. Associations between ESR and CRP level were determined using the Pearson correlation coefficient.

Results: The leading diagnosis associated with extreme ESR elevations (n [%]) was infection (1932 [40]), followed by autoimmune (1839 [38]) and malignancy (1736 [36]) ($P<.01$). Extreme elevations in ESR varied by sex, with higher ESRs in men (mean, 117±13.3 mm/h) than in women (mean, 115.9±12.5 mm/h) ($P=.008$). Extreme ESR elevations correlated inversely with the CCI ($P=.008$) and did not correlate with the CRP level. There were no correlations between extreme elevations in ESR and age or race.

Conclusion: We found that almost all patients have an identifiable etiology for extreme ESR elevations and that infection is the most common disease association. Unlike previous research, we identified higher ESRs in men than in women and no associations with age, race, and comorbid illness. These findings may enhance the diagnostic evaluation of patients with extreme ESR elevations.

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The erythrocyte sedimentation rate (ESR) is a laboratory test that represents the distance in millimeters that red blood cells descend in a tube over 1 hour. Inflammation causes the cells to form dense clumps, which descend more rapidly than individual cells. The ESR has long been used as a marker of "sickness."[1-3] Although moderate elevations in ESR may occur without a known cause, extreme elevations of 100 mm/h or greater are typically associated with malignancy, infection, or inflammation.[1,4] Extreme elevations in ESR have been shown to have a positive predictive value of 90% when correlating with certain diagnoses.[1,4] These diagnoses have been categorized into infection, autoimmune, malignancy, renal disease, or miscellaneous.[5] Research has reported variable results on associations between diseases and extreme elevations in ESR.[1,4-15]

An initial study from Mayo Clinic found that malignancy was the most common reason for ESR greater than 100 mm/h.[5] Nonetheless, this study involved a small sample of 263 patients.[5] Since then, additional studies of similar scale have found that infections result in extreme elevations in ESR more often than malignancy.[1,4-15] Despite these findings, physicians continue to associate extremely elevated ESR of unknown cause with malignancy.[14] To date, there have been no large-scale studies to examine potential diseases related to extremely elevated ESR.

The ESR has also been coupled with patient characteristics such as age, sex, and race.[1,2,6,16-18] Research has found that normal

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ESR ranges increase with age.[3,16,19] With regard to sex, women may have a higher normal ESR range than men.[2,17] There is also limited evidence that race may affect ESR; according to 1 study, Africans were more likely to have elevated ESRs than whites.[1] However, less is known about associations between these patient-related factors and extreme elevations in ESR, because most previous studies have involved normal ESR ranges.[1,2,6,16-18] Further research may be needed to better clarify relationships between extremely elevated ESR and patient age, sex, and race.

Extreme elevations in ESR are said to be a sensitive indicator of disease.[1] Furthermore, evidence suggests that extreme elevations in ESR indicate a poor prognosis.[1,4,20] However, little is known about degrees of illness and comorbidity in patients with extremely elevated ESRs.[1,4] The Charlson Comorbidity Index (CCI) is a recognized indicator of mortality[21] and is a useful gauge of illness severity. There is also evidence that certain diseases may result in ESR, but not C-reactive protein (CRP) level, elevations. Moreover, correlations between ESR and CRP level are uncertain.[22,23] Some have recommended using both CRP level and ESR when evaluating patients, as CRP level may be more sensitive.[24] Therefore, we elected to assess potential relationships between extreme elevations in ESR, CRP level, and illness severity by using the CCI.[21]

Multiple studies have examined an ESR of 100 mm/h or greater in relation to certain diagnoses,[5,14] as well as sex, age, and race.[1,2] However, there is a need for large-scale investigations with a comprehensive selection of variables to understand extreme ESR elevations. Therefore, we retrospectively studied associations between extremely elevated ESR and characteristics of disease, age, sex, race, CCI, and CRP level in a large sample of patients over a 10-year time frame.

PATIENTS AND METHODS

This was a retrospective chart study of patients older than 18 years with an ESR of 100 mm/h or greater examined at Mayo Clinic, Rochester, Minnesota, from January 1, 2002, through December 31, 2011. Over this time frame, patients were identified on the basis of their first elevation in ESR of 100 mm/h or greater.

Data Abstraction

Patient records were examined by 2 independent reviewers to determine diagnoses associated with the elevated ESR up to a year after the first ESR was identified. To ensure reliability, the 2 raters (L.M.D. and J.A.F.) reviewed the same convenience sample of 100 patients, and interrater agreement was calculated using the intraclass correlation coefficient. The agreement across all individual disease categories (intraclass correlation coefficient; 95% CI) were as follows: infection (0.98; 0.93-1.00), inflammatory/autoimmune (0.86; 0.76-0.96), hematology-oncology (0.80; 0.68-0.92), renal disease (0.82; 0.68-0.97), miscellaneous (0.73; 0.51-0.96), and unknown (1.00; 1.00-1.00). After exhibiting excellent agreement, the raters then proceeded to abstract data from patient records independently. Manual reviews of electronic medical records included evaluation of clinical notes, pathology reports, and radiology reports for the year after the initial extreme elevation in ESR. Diagnoses were retained if the provider specifically attributed a diagnosis to be associated with the elevated sedimentation rate, if the diagnosis was known in the literature to be associated with the elevated sedimentation rate, or if the reviewer thought the diagnosis was likely associated. As done in more recent studies, if a patient had more than 1 diagnosis associated, each diagnosis was included.[9] Categories were divided as in previous studies into infection, inflammatory/autoimmune, malignancy, renal disease, miscellaneous, and unknown.[1,5,7,8] A subset analysis evaluated specific diagnosis within each category. The top 5 diagnoses from each category were then determined.

Statistical Analyses

Descriptive summaries were reported as mean ± SD for continuous variables and as frequency (percentage) for categorical variables. To assess the associations between extreme ESR elevations (≥100 mm/h) and diseases, we first ranked disease subcategories (eg, pneumonia and cellulitis) within each of the disease categories (eg, infection). In this analysis, patients with the presence of a particular disease subcategory, with or without the presence of additional disease subcategories, were considered as "with disease" and patients without the particular disease subcategory were considered as "without disease." Comparisons of ESR values between patients with and without disease were performed using the Wilcoxon rank sum test. A similar analysis